

March 28, 1948.

Dr. Nils Fries,
Institute of Physiological Botany,
University of Uppsala,
Sweden.

Dear Nils,

First, let us thank you for sending us that interesting brochure of photographs of Sweden. We enjoyed it very much.

Since the Fall, of course, we have been installed here, and must confess to finding the move a good one. Our present laboratory facilities are temporary, while a remodelled space is being outfitted for permanent use, but we have been able to accomplish a good deal nevertheless. Esther is enrolled as a student, and is working on the genetic control of mutability in "mutable" mutants of *E. coli* K-12, while I have been occupied with a study of the gene-enzyme relationship, using ultra-violet induced lactose-negative mutants as material.

What chemical work has been done points to the activity of a simple, single lactose-hydrolysing enzyme in this organism, and I wish I could write that the genetic control of this enzyme were simple, as one might expect on the "one-to-one" theory, but, alas it is not so. Some eight different loci are involved in the two or three hundred lactose-negative mutants so far studied, and there may be more. In *coli* K-12, at any rate, it looks like this enzyme is subject to the control of many genes. On the other hand, some of the mutations are apparently pleiotropic, even on the enzymatic level, - single mutations affecting several enzymes involved in carbohydrate metabolism. Further chemical work may uncover an improbably complex metabolic scheme that would vitiate these remarks, but at the moment I must conclude that the study of mutations can give no certain information on the physical mechanisms of gene action. A single gene may confer specificity on a single enzyme, but it may also alter the cell economy in some subtle way that ~~it~~ may prevent the appearance of other enzymes.

Of course, all this work has been on *E. coli*, and I am sure that everyone would feel a lot happier to see a similar study on other organisms with a more securely established sexual stage-- and I ~~propose~~ propose to do this either with *Neurospora* or with *Ophiostoma*. May I ask you now to send me some of your more vigorous wild type and mutant strains. In particular have you paid any attention to the carbohydrate metabolism of *Ophiostoma*? Do you know which sugars it can utilize for growth, and what the most prominent metabolic products may be? Have you made any attempt at enzyme studies in this fungus? Be sure to let us know how you have been and what you occupy yourself with now. Father sends her best regards.

Yours sincerely,

Joshua Lederberg
Assistant Professor of Genetics